Spreading of Cells Flowing in a Straight Microchannel

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論 文 内 容 の 要 旨

Chapter 1 Introduction

Various experiments showed an effort to understand cellular flow behavior in microscopic to macroscopic flow phenomena. One example is a development of techniques to explain Fahraeus-Lindqvist effect in a very narrow vessel. Two major characteristics of cells are deformability and mobility. Deformability is an important characteristic of red blood cells (RBCs), given that RBCs need to flow through narrower capillary than their diameter. Motility is an important characteristics of microorganisms, given that the cells can migrate toward light, gravity and chemicals for their metabolism. Over the years, there were several studies about mass transport as well as technical issues involved in mixing or separating cells in biomedical microdevices. In the field of micro total analysis system, there are increased opportunities to manipulate, stimulate or diagnose high concentration cells in microfluidics. Nowadays the spreading of rigid particles in a microchannel under diluted solution conditions is clearly understood. However, the spatial distribution and the mixing of cells under high concentration in the microscale flow is still difficult to perform quantitative detailed measurements. Moreover, spatial distribution and the mixing of motile cells are not clearly understood. The aim of this thesis is to investigate the effects of deformability and motility of cells on the spanwise spreading of cells flowing in a straight microchannel. I investigate experimentally the collective spreading of RBCs or *Chlamydomonas reinhardtii* (*C. reinhardtii*) in the bifurcated polydimethylsiloxane (PDMS) microchannel. I measured how the initially inhomogeneous distribution of RBCs or *C. reinhardtii* changes while flowing, and discussed the spreading process. The thesis consists of 5 chapters. In chapter 1, I explain the background, former understanding and purpose of the study. I will introduce the microchannel in the chapter 2. In chapter 3, I investigated the effect of cell's deformability by using a red blood cell (RBC) as a model cell. I experimentally investigated the collective spreading of red RBCs in a straight microchannel. In chapter 4, I investigated the effect of cell's motility by using *C. reinhardtii* as a model cell. I experimentally investigated the behaviors of motile *C. reinhardtii* in a straight microchannel, and measured how cells spread in the spanwise direction during downstream flow. In chapter 5, I conclude the study.

Chpater 2 Bifurcated PDMS microchannel

For the decades, miniaturized instrumentation has attracted great interest in the world. Nodaway the researches of integrated microfluidic devices are referred to as lab-on-a-chip devices or micro total analysis systems (**μ**TAS). For instance, fluid handling, microreactors, separation systems, cell handling, and cell culturing. The advantages of microchip or microdevice are lower in cost, consume less material sample, and minimally invasive to the biological application. According to the above advantages, some microdevices could be designed as disposable to avoid contamination. Moreover, the laws under macro system might be applied directly to the

micro system; for instance, the Fahraeus-Lindqvist effect (Fahraeus and Lindqvist 1931) in the micro system. It is based on the Fahraeus effect in the macro system. Therefore, it still has many differences and needs to understand. In the thesis, I fabricated PDMS mold by replicating SU-8-50 (MicroChem, Newton, MA) molds. SU-8 was negative photoresist with high transparency and usually used to fabricate high-aspect-ratio microfluidics mold. After a series of soft lithography, SU-8 structures on the silicon wafer could be as mold for replication. I would introduce the detailed steps behind the chapter.

Chpater 3 Collective spreading of red blood cells flowing in a microchannel

Controlling the concentration of RBCs at given position across the width of a channel is an important aspect in the design of microfluidic devices. Despite its biomedical importance, the collective spreading of RBCs in a microchannel has not yet been fully clarified. Therefore, I experimentally investigated the collective spreading of RBCs in a straight microchannel. I measured changes from the initially inhomogeneous distribution of RBCs during flow, and investigated the spreading process. I also proposed scaling arguments, which clarified the basic mechanism of the spreading process.

Chapter 4 Behavior of motile unicellular flowing in a microchannel

Microorganism plays a vital role in many biological, medical and engineering phenomena. Recently, in understanding cell's behaviors at the cellular scale, microfluidics has been used by some researches. In this charter, therefore, I use *Chlamydomonas reinhardtii* as a model microorganism, which is a unicellular alga with two flagella for swimming. I changed the RBCs to *C. reinhardtii* , because the size of *C. reinhardtii* is similar to RBCs. *C. reinhardtii* has not only cell wall as rigid body but flagella for swimming. I discuss how cells are spread or directed in the microchannel by interacting with the background flow, in a similar manner to the previous chapter.

Chpater 5 Conclusions and future directions

The thesis consists of mainly two parts. In the first part, in the chapter 3, I used red blood cells (RBCs) to see the effect of cell's deformability. I could observe RBCs with Hct = 20 and 40% reached the right side wall within the half length of microchannel. The collective dispersion coefficient was proportional to the hematocrit and flow rate, and followed standard diffusion scaling. The spreading process was diffusive and mainly caused by cell-cell interactions. The knowledge obtained in this study will be useful in understanding collective behaviors of RBCs in a microchannel and microcirculation. The second part of the thesis, i.e. chapter 4, focused on the motility of cells. I investigated the behaviors of motile algae *C. reinhardtii* in a microchannel. I measured how cells spread in the spanwise direction during downstream flow. I showed that cells spread almost ballistic in the spanwise direction under high flow rate conditions, and reached plateau at a certain distance. Interestingly, in low flow rate condition, cells tended to direct toward upstream. The mechanism can be explained hydrodynamically, and the tendency can be regarded as negative rheotaxis. These findings are important in handling or separating motile cells in microfluidics. In this thesis, I investigated the effects of deformability and motility of cells on the spanwise spreading of cells flowing in a straight microchannel. The results showed that deformability and motility of cells have considerable influence on the spreading of cells. I believe that the obtained results are useful in designing a microfluidic device to manipulate, stimulate and diagnose cells. Moreover, The research of the thesis provides the basis for further research. A few of possible research topics from the thesis could be addressed in the future.